REMARKS

Claims 1-6, 8-14, 16, 20-23, 49-52, 66-68, 74-97, and 121-127 were pending, with claim 12 withdrawn. With this amendment, claims 1-2, 4, 8-9, 13, 16, 20-23, 81, 91, 95 and 121-123 have been amended. Claims 81 and 91 were amended to correct for typographical errors while claim 95 was amended to correct for antecedent basis. Support for the amendments to claims 1-2, 4, 8-9, 13, 16, 20-23, and 121-123 is found in the following table.

Claim	Support in specification.
1. (Currently amended) A method for constructing a variant set for <u>modifying</u> an antibody of interest, the method comprising: (a) identifying a plurality of positions in said antibody of interest and, for each respective position in said plurality of positions, one or more substitutions for the respective position, wherein the plurality of positions and the one or more substitutions for each respective position in the plurality of positions collectively define an antibody sequence space; (b) selecting a first plurality of variants of the antibody of interest, thereby forming a variant set, wherein said variant set comprises a subset of said antibody sequence space; (c) measuring a property of all or a portion of the variants in said variant set;	Section 5 beginning on page 11, line 1, and Figure 2
(d) modeling <u>on a computer</u> a sequence-activity relationship between (i) one or more substitutions at one or more positions of the antibody of interest in the variant set and (ii) the property measured for each variant in all or said portion of the variants in the variant set, and then deriving	Section 5.1, beginning on page 14, line 5, and Figure 1
from the sequence-activity relationship [[:]] (A) a ~~plurality of first values, wherein each respective first value in the plurality of first values is~~ <u>first value for a</u> ~~the~~ contribution to the measured property by <u>the</u> one or more substitutions at	Page 13, lines 4-6; page 60, lines 7-27; Figures 4 and 5

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one or more positions in the plurality of positions in the antibody of interest, and (B) a <u>second value</u> ~~plurality of second values, wherein each second value in the plurality of second values quantifies~~ <u>quantifying</u> a confidence <u>with which the contribution to the measured property by the one or more substitutions at one or more positions of the antibody of interest can be assigned</u> ~~of a first value in the plurality of first values~~; <u>and</u> ~~(e) redefining said variant set to comprise variants in said antibody sequence space that include substitutions in said plurality of positions that are selected based on a function of said plurality of first values and said plurality of second values;~~ ~~(f) measuring a property of all or a portion of the variants in said variant set after said variant set has been redefined in step by said redefining (e); and~~ <u>(e)</u> ~~(g)~~ outputting <u>said first value and said second value</u> ~~a property of all or a portion of the variants in said variant set~~ to a user, a display, or <u>a tangible computer readable storage medium</u> ~~other output device~~.	Figure Element 26 of Figure 1; page 14, lines 16-17; element 14 of Figure 1, page 14, lines 10-11, element 36 of Figure 1, page 14, lines 12-15
2. (Currently amended) The method of claim 1, the method further comprising repeating said <u>(b)</u> selecting<u>,</u> measuring (c), <u>and</u> said modeling (d)~~, said redefining (e), and said measuring (f)~~ until a variant in said variant set exhibits a value for said property that exceeds a predetermined value.	Steps 4, 5, 7 and 8 of Figure 2; page 12, lines 28, through page 14, line 2
4. (Currently amended) The method of claim 1, the method further comprising repeating said <u>(b)</u> selecting<u>,</u> measuring (c), <u>and</u> said modeling (d)~~, said redefining (e), and said~~	Steps 4, 5, 7 and 8 of Figure 2; page 12, lines 28, through page 14, line 2

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measuring (f) until a variant in said variant set exhibits a value for said property that is less than a predetermined value.	
8. (Currently amended) The method of claim 1, wherein each said first value in said plurality of first values describes a relationship between the property measured by said measuring (c) and: (i) a substitution at a position in said plurality of positions represented by all or said portion of the variants in said variant set, (ii) a plurality of substitutions at a position in said plurality of positions represented by all or said portion of the variants in said variant set, or (iii) one or more substitutions in one or more positions in said plurality of positions represented by all or said portion of the variants in said variant set.	Corrected for antecedent basis in view of amendments to claim 1
9. (Currently amended) The method of claim 8, wherein said modeling comprises regressing: $$V_{measured} = W_{11}P_1S_1 + W_{12}P_1S_2 + \ldots + W_{1N}P_1S_N + \ldots + W_{M1}P_MS_1 + W_{M2}P_MS_2 + \ldots + W_{MN}P_MS_N$$ wherein, $V_{measured}$ is the property measured in all or said portion of the variants in said variant set by said measuring (c); W_{MN} is a contribution to a measured property by one or more substitutions at one or more positions in the plurality of positions of the antibody of interest a value in said plurality of first values;	Corrected for antecedent basis in view of amendments made to claim 1

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P_M is a position in said plurality of positions in said antibody of interest; and S_N is a substitution at a position in the plurality of positions in said antibody of interest.	

13. (Currently amended) The method of claim 1, the method further comprising ~~wherein said~~ redefining <u>said variant set to comprise variants in said antibody sequence space that include substitutions in said plurality of positions that are selected based on a function of said first value and said second value by</u> ~~(e) further comprises~~:
 	
    computing~~, for each respective first value in the plurality of first values,~~ a modified ~~respective~~ first value by modifying the ~~respective~~ first value based on a function of [[a]] <u>the</u> second value~~, in the plurality of second values, that corresponds to the respective first value, thereby computing a plurality of modified first values~~; and
 	
    computing a predicted score, for each respective variant in a population of variants of said antibody of interest, using the ~~plurality of~~ modified first <u>value</u> ~~values, thereby computing a plurality of predictive scores,~~ wherein each variant in said population of variants includes a substitution at one or more positions in said plurality of positions in said antibody of interest; and
 	
    redefining said variant set by selecting variants from among said population of variants as a function of the predicted score received by each variant in said set of variants.
	Claim 1 as originally filed;
	Figure 13, lines 11-13
	
	Amended to correct for antecedent basis in view of amendments to claim 1
	
	Amended to correct for antecedent basis in view of amendments to claim 1

16. (Currently amended) The method of claim <u>13</u> [[1]], wherein said redefining ~~(e) further~~ comprises redefining said variant set to comprise one or more variants of the	Amended to correct for antecedent basis in view of amendments to claim 1

antibody that are not in the antibody sequence space of said identifying (a).	
20. (Currently amended) The method of claim 13 [[1]], wherein said redefining (e) further comprises redefining said variant set to comprise one or more variants each having a substitution in a position in said plurality of positions not present in any variant in the variant set selected by said selecting step (b).	Amended to correct for antecedent basis in view of amendments to claim 1

21. (Currently amended) The method of claim 5, wherein the contribution of each respective rule in said plurality of rules to the defining of said antibody sequence space is independently weighted by a rule weight in a plurality of rule weights corresponding to the respective rule, ;-and the method further comprising, prior to said redefining (e), the method comprising:
 	
         adjusting one or more rule weights in said plurality of rule weights based on a comparison, for each respective substitution at each position in the plurality of positions in the variant set, of (i) a value derived for the respective substitution from the sequence-activity relationship, and (ii) a score assigned by the plurality of rules to the respective substitution; and
 	
         repeating said identifying step using said rule weights, thereby redefining said plurality of positions and, for each respective position in said plurality of positions, redefining the one or more substitutions for the respective position; and wherein
 	
         said redefining step (e) further comprises redefining said variant set to comprise one or more variants that are not in the subset of the antibody sequence space
	Amended to correct for antecedent basis in view of amendments to claim 1

formed in ~~defined in~~ said <u>selecting</u> ~~step~~ (b).	
22. (Currently amended) The method of claim 1 wherein said modeling (d) further comprises modeling a plurality of sequence-activity relationships, wherein each respective sequence-activity relationship in said plurality of sequence-activity relationships describes the relationship between (i) one or more substitutions at one or more positions of the antibody of interest represented by the variant set and (ii) the property measured for all or said portion of the variants in the variant set; ~~and~~ <u>the method further comprising:</u> ~~said redefining (e) comprises~~ redefining said variant set ~~to~~ <u>to form a redefined variant set that comprises</u> ~~comprise~~ variants that include substitutions in said plurality of positions that are selected based on a combination function of said plurality of sequence-activity relationships.	Amended to correct for antecedent basis in view of amendments to claim 1
23. (Currently amended) The method of claim 22, the method further comprising: repeating said measuring (c) based upon a property of all or a portion of the variants in said redefined variant set ~~of said redefining (e)~~; and weighting each respective sequence-activity relationship in said plurality of sequence activity relationships based on an agreement between (i) measured values for the property of variants in said redefined variant set and (ii) values for the property of variants in said redefined variant set that were predicted by said respective sequence-activity relationship, wherein a first sequence-activity relationship that achieves better agreement between measured and predicted	Amended to correct for antecedent basis in view of amendments to claim 1

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values than a second sequence-activity relationship receives a higher weight than said second sequence-activity relationship.	
121. (Currently amended) The method of claim 1, wherein [[a]] the second value in the plurality of second values is a standard deviation of a corresponding the first value in the plurality of first values.	Amended to correct for antecedent basis in view of amendments to claim 1
122. (Currently amended) The method of claim 13 [[1]], wherein each variant in the redefined variant set of (e) differs by fewer than 5 substitutions from at least one variant for which the property has been measured in said measuring (c).	Amended to correct for antecedent basis in view of amendments to claim 1
123. (Currently amended) The method of claim 1, the method further comprising wherein said redefining of said variant set (e) further comprises: computing a modified first value in the plurality of first values by modifying the first value based on a function of the second value, in the plurality of second values, that corresponds to the first value, thereby computing a plurality of modified first values; and wherein said function of said plurality of first values and said plurality of second values comprises using the modified first value for each of the one or more substitutions at the plurality of positions as a basis for including or excluding substitutions from the redefined variant set.	Amended to correct for antecedent basis in view of amendments to claim 1

Accordingly, no new matter has been added by way of the amendments to the claims.

In the Office Action mailed July 10, 2008, the Examiner imposed the following species election requirement:

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D)   A further step to those selected in claim 1, selected from those in claims 2, 3, 4, 13, 16, 20, 21, 22, or 23;

E)   A property measuring step, from those in claims 49-51, 81, 82, 83, 84, 85, 87, 89, 91, 92, 93, or 94;

Applicants hereby provisionally elect, with traverse, for species requirement D, the redefining step as further recited in claim 13. Claims 1-6, 8-14, 16, 20-23, 49-52, 74-97, and 121-126 are believed to be readable upon this elected species. Claims 1-6, 8-14, 16, 20-23, 49-52, 74-97, and 121-126 are believed to be generic to this elected species.

Applicants hereby provisionally elect, with traverse, for species requirement E, the property measuring step recited in claim 89. Claims 1-6, 8-14, 16, 20-23, 49-52, 74-80, 89-90, and 121-126 are believed to be readable upon this elected species. Claims 1-6, 8-14, 16, 20-23, 49-52, 74-80, and 121-126 are believed to be generic to this elected species.
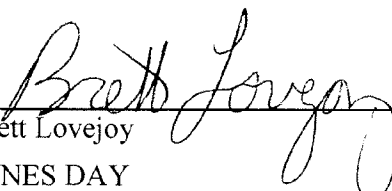
Applicants respectfully request that the above-mentioned amendments and remarks be entered and made of record in the file history of the subject application.

CONCLUSION

Applicants respectfully request entry of the foregoing amendments and remarks into the file of the above-identified application. If any fees are due in connection with this submission, please charge the required fee to Jones Day Deposit Account No. 50-3013.

Respectfully submitted,

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